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(54) Title: **METHOD FOR HLA TYPING**

(57) Abstract: A method for the identification of DNA sequence elements in complex and highly variable sequences is described. The method consists of identifying a short sequence element of several DNA bases (2-6 bases) at a given position in the genome simultaneously on all parental alleles. The method allows differentiating mini-haplotypes on different alleles in one analysis. The method consists of carrying out an enzymatic primer extension reaction with a combination of extension primers (pool of primers) and analysing the products by mass spectrometry. The pool of primers is assembled in such a way that the primer extension product allows unambiguous identification of both the primer of the pool that was extended and the base that was added. The method is of great utility for DNA sequences harbouring many SNPs close to each other with many possible haplotypes. Such sequences are known in the Major Histocompatibility Complex (MHC). This method is particularly well suited for DNA-based HLA typing and in combination with a suitable selection of sites tested, it is superior in ease of operation to conventional HLA typing methods. We have identified sets of these assays for HLA-A, HLA-B, and HLA-DRB 1 that allow unambiguous four-digit HLA of each of these genes with between 11 and 28 queried markers.



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